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## PATENT SPECIFICATION

NO DRAWINGS

923,400



Date of Application and filing Complete Specification: Aug. 30, 1961.

No. 31212/61.

Two Applications made in Switzerland (Nos. 10087 and 10088) on Sept. 7, 1960.

Complete Specification Published: April. 10, 1963.

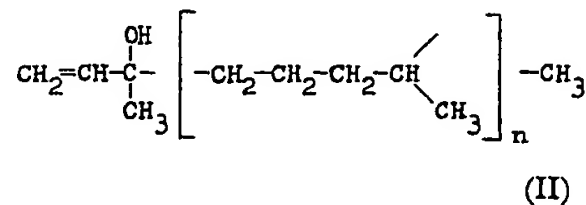
Index at acceptance:—Classes 2(3), C3A13A4(A1:F1:K); and S1(1), L(1:4).

International Classification:—C07c. (A61k).

## COMPLETE SPECIFICATION

Aliphatic Triols, a process for their manufacture and  
Cosmetic preparations containing same

We, F. HOFFMANN-LA ROCHE & Co.,  
AKTIENGESELLSCHAFT, a Swiss Company of  
124—184 Grenzacherstrasse, Basle, Switzer-  
land, do hereby declare the invention, for  
5 which we pray that a patent may be granted  
to us, and the method by which it is to be  
performed, to be particularly described in  
and by the following statement:—



## ERRATA

## SPECIFICATION NO. 923,400

Page 1, Heading, for "C07C. (A61k)." read "C07C(A61k)."

Page 3, line 58, for "crystallises" read "crystallizes"

Page 3, line 125, for "hydroxy" read "dihydroxy"

THE PATENT OFFICE,  
16th May 1963

DS 73748/1(8)/R.109 200 5/63 PL

(I)

ammonia.

Useful starting compounds of formula II  
include isophytol, tetrahydro - nerolidol  
[3,7,11 - trimethyl - 3 - hydroxy - dodecaene-  
(1)] and dihydro - linalool [3,7 - dimethyl-  
3 - hydroxy - octaene - (1)]; the first two  
being preferred. 50

wherein  $n$  is 1,2 or 3. They have properties  
which render them useful as emulgators and  
solubilizers; especially useful in the cosmetic  
art, particularly in cosmetic preparations for  
the treatment of skin and hair. The preferred  
compounds are 3,7,11,15-tetramethyl-1,2,3-  
trihydroxy-hexadecane, 3,7,11-trimethyl-1,2,3-  
trihydroxy-dodecane and 3,7-dimethyl-1,2,3-  
trihydroxy-octane. 20 25

The process of the invention is carried out  
by reacting a compound having the formula:

The process of the invention may involve  
several intermediates. The following formula  
scheme illustrates an embodiment of the pro-  
cess in which monoester, epoxy-ester and  
diester intermediates are formed and in which  
aliphatic carboxylic acids containing up to  
seven carbon atoms or benzoic or alkyl-sub-  
stituted benzoic acids on the one hand and  
aliphatic peracids containing up to seven  
carbon atoms or benzoic or alkyl-substituted  
benzoic peracids on the other hand are used: 55 60

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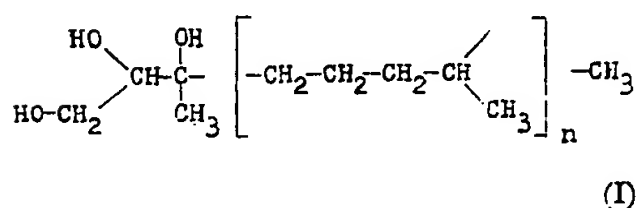
## COMPLETE SPECIFICATION

### Aliphatic Triols, a process for their manufacture and Cosmetic preparations containing same

We, F. HOFFMANN-LA ROCHE & Co., AKTIENGESELLSCHAFT, a Swiss Company of 124—184 Grenzacherstrasse, Basle, Switzerland, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

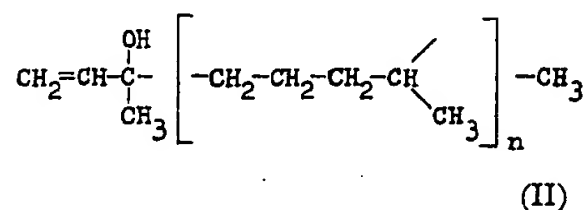
The present invention relates to aliphatic triols; more particularly, it is concerned with aliphatic 1,2,3-triols, with a process for their manufacture and with cosmetic preparations containing same.

The aliphatic triols of the invention have the formula:



wherein  $n$  is 1,2 or 3. They have properties which render them useful as emulgators and solubilizers; especially useful in the cosmetic art, particularly in cosmetic preparations for the treatment of skin and hair. The preferred compounds are 3,7,11,15-tetramethyl-1,2,3-trihydroxy-hexadecane, 3,7,11-trimethyl-1,2,3-trihydroxy-dodecane and 3,7-dimethyl-1,2,3-trihydroxy-octane.

The process of the invention is carried out by reacting a compound having the formula:



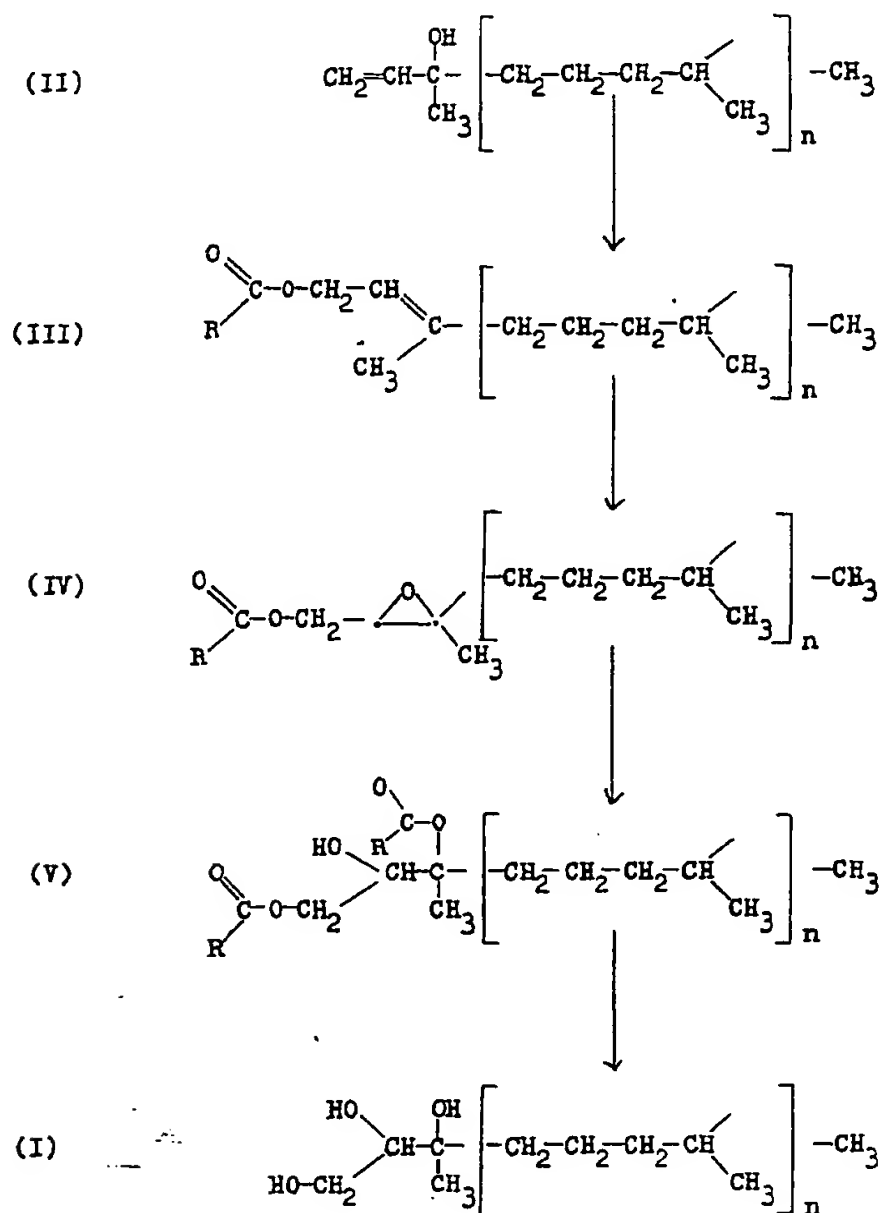
wherein  $n$  is 1,2 or 3, with an organic peracid in the presence of the carboxylic acid corresponding to said peracid and hydrolyzing the reaction product.

The organic peracids employed in the process of the invention are preferably aliphatic peracids containing up to seven carbon atoms (e.g. performic acid, peracetic acid and perpropionic acid, preferably performic acid). However, aromatic peracids such as perbenzoic acid and alkyl-substituted perbenzoic acids may also be employed.

The hydrolyzing agents employed in the process of the invention are aqueous alkaline agents; for example, aqueous alkalis (e.g. sodium hydroxide or potassium hydroxide solutions) or, preferably, concentrated ammonia.

Useful starting compounds of formula II include isophytol, tetrahydro - nerolidol [3,7,11 - trimethyl - 3 - hydroxy - dodecaene - (1)] and dihydro - linalool [3,7 - dimethyl - 3 - hydroxy - octaene - (1)]; the first two being preferred.

The process of the invention may involve several intermediates. The following formula scheme illustrates an embodiment of the process in which monoester, epoxy-ester and diester intermediates are formed and in which aliphatic carboxylic acids containing up to seven carbon atoms or benzoic or alkyl-substituted benzoic acids on the one hand and aliphatic peracids containing up to seven carbon atoms or benzoic or alkyl-substituted benzoic peracids on the other hand are used:



In formulae III, IV and V the R group depends on the particular peracid employed and is either hydrogen, a C<sub>1-6</sub> alkyl group or a phenyl or alkyl-substituted phenyl group. The symbol *n* stands for 1,2 or 3.

The first step of the embodiment of the process shown in the formula scheme (i.e. converting compounds of formula II to esters of formula III) is carried out by treating the compounds of formula II with a concentrated aliphatic or aromatic carboxylic acid corresponding to the peracid to be employed. The peracid is then introduced into the reaction mixture and results in the formation of the epoxy-ester IV which, in the presence of the concentrated carboxylic acid, is converted into a diester of formula V. It is preferable to allow the allylic rearrangement of the ester precursors of the esters of formula III to take place almost completely before the epoxidation with the peracid is commenced. This can suitably be carried out by reacting the starting material first with the aliphatic

carboxylic acid alone until complete allyl rearrangement has taken place, and then introducing hydrogen peroxide into the mixture to form the peracid *in situ*. This step is preferably carried out at room temperature, although slightly higher temperatures (for example, up to about 40°C) can be employed. At 40°C the reaction is complete in a few hours.

Hydrolysis of compounds of formula V to form compounds of formula I is carried out as mentioned earlier with alkaline hydrolyzing agents. Concentrated ammonia is preferred since the excess ammonia and the water can easily be removed by reducing the pressure. A viscous oil, readily soluble in ether, is thereby obtained. It can easily be separated from any ammonium salts formed in the hydrolysis by treatment with water. The hydrolysis product is fit for direct use but it can be purified by molecular distillation if desired.

The following examples are illustrative of the process:

## EXAMPLE 1

5 Into a reaction vessel containing a stirrer, thermometer, and dropping funnel, 200 g of isophytol and 570 ml of concentrated formic acid are added and the homogeneous mixture stirred for 2 hours at 40°C. Thereafter, the reaction mixture is cooled to 20°C and, during the course of 15 minutes, a solution of 83 g of 30 weight per cent hydrogen peroxide and 11 ml of water is added thereto. The temperature of the reaction mixture climbs slowly and is maintained at 40°C with the help of an ice-bath. Since the temperature, after about 1 hour, falls below 40°C without cooling, the mixture is maintained at 40°C for another 2 hours with the help of a water-bath. Thereafter the reaction mixture is poured into a mixture of 1 litre of ice-water and 500 ml of ether. The aqueous layer is removed and the ether solution washed twice, each time with 150 ml of water. The ether is removed and the residue treated with 300 ml of concentrated ammonia (25%). The resulting mixture is shaken well and then allowed to stand for 15 minutes at room temperature. The water and the ammonia are then removed in a rolling evaporator at 50°C by use of a water-pump, and the viscous residue taken up in 1500 ml of ether. The ether solution is washed 3 times, each time with 200 ml of water, dried over sodium sulphate, filtered, and the ether evaporated off. 220 g of 3,7,11,15 - tetramethyl - 1,2,3-trihydroxy - hexadecane [dihydroxy - dihydro-phytol] are thus obtained as a bright yellow, viscous oil boiling at 130°C/0.01 mm.

## EXAMPLE 2

40 150 g of 3,7,11 - trimethyl - 3 - hydroxy-dodecaene-(1) are treated as in Example 1 with 570 ml of concentrated formic acid, then with a solution of 83 g of hydrogen peroxide and 11 ml of water, and worked up as in Example 1. 155 g of 3,7,11-trimethyl - 1,2,3 - trihydroxy - dodecane are obtained in the form of a bright yellow viscous oil which is distilled under high vacuum; b.p. 146°C/0.07 mm.

## EXAMPLE 3

50 105 g of 3,7 - dimethyl - 3 - hydroxy-octaene-(1) is treated with 570 ml of concentrated formic acid, then with a solution of 83 g of hydrogen peroxide and 11 ml of water, and worked up according to the procedure of Example 1. 107 g of 3,7-dimethyl-1,2,3 - trihydroxy - octane are obtained in the form of a bright yellow oil which distills in high vacuum; b.p. 115°C/0.07 mm. The product crystallises upon standing at room temperature.

60 The favourable properties of the triols which render them specially useful as cosmetic agents are to be found in the fact that they strongly adhere to the skin and hair,

that they are not gummy or oily and that they leave the hair and skin soft and velvety. Further they form an invisible, water-repellant, protective layer over the skin, yet at the same time do not interfere with the skin's respiration. Yet further, they are very stable and can be used in the form of emulsions, salves and lotions. They can also be combined with other active ingredients, such as vitamins, hormones, fungicides, and bactericides.

The concentration of the triols employed to form the skin and hair preparations is in the range of from 0.1 to 10 per cent by weight based on the weight of the preparation. However, since the desired cosmetic activity is already evident at concentrations as low as 0.1 per cent, from 0.1 to 3 per cent is preferred.

The other ingredients to make up the skin and hair preparations of the invention (e.g. skin and hair lotions, creams, salves and emulsions) are conventional in the cosmetic art.

The following examples are given by way of illustration of the way in which the cosmetic preparations of the invention may be prepared.

A. For the preparation of toilet water, 0.5 g of dihydroxy - dihydro phytol and 0.5 g of pantothenyl alcohol are dissolved in 49 g of 96% ethyl alcohol and mixed with 50 g of water. The resulting solution can be perfumed as desired.

B. 0.5 g of dihydroxy - dihydro - phytol is mixed with 0.5 g of pantothenyl alcohol, 10.0 g of a 1 per cent polyacrylic acid solution in water, 0.1 g of triethanol amine and 88.9 g of water. The resulting mixture is useful as a facial lotion to which perfume can be added as desired.

C. 1.0 g of dihydroxy - dihydro - phytol is mixed with 1.0 g of 3,7 - dimethyl - 1,2,3-trihydroxy-octane, 1.0 g of hydroxyethylated oleyl alcohol, 10.0 g of 96 per cent ethyl alcohol and 87.0 g of a 1% alginate solution in water. The resulting mixture, which is useful as a hand lotion, can be perfumed as desired.

D. 1.0 g of dihydroxy - dihydro - phytol and 1.0 g of 3,7,11 - trimethyl - 1,2,3 - trihydroxy-dodecane are mixed with 1.0 g of 3,7 - dimethyl - 1,2,3 - trihydroxy - octane, 0.5 g of pantothenyl alcohol and 26.5 g of 96% ethyl alcohol. After suitable addition of perfume, the mixture is mixed with 90 g of a commercial aerosol gas mixture (such as chlorinated or fluorinated hydrocarbons) and introduced into an aerosol atomizer. The resulting spray preparation can be used as a hand or skin lotion.

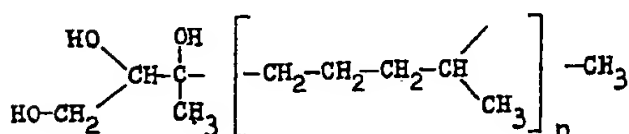
E. 3.0 g of polyvinyl-pyrrolidone are mixed with 0.5 g of hydroxy - dihydro - phytol, 0.2 g of pantothenyl alcohol, 46.3 g of 96% ethyl alcohol (or isopropyl alcohol) and 50.0 g of water and the resulting mixture perfumed

as desired. The resulting cosmetic preparation is especially useful as a hair tonic, rendering the hair easy to comb.

- 5 F. 0.3 g of 3,7,11 - trimethyl - 1,2,3-trihydroxy-dodecane is mixed with 0.3 g of 3,7 - dimethyl - 1,2,3 - trihydroxy - octane, 0.5 g of pantothenyl alcohol, 0.2 g of N,N-bis[1 - methyl - 3 - (2,2,6 - trimethyl - cyclo-
- 10 hexadecyl) - propyl] - N,N - dimethyl - 1,6-hexadecylamine-bis methochloride, 49.0 g of 96% ethyl alcohol (or isopropyl alcohol) and 50.0 g of water. The resulting hair tonic can be perfumed as desired.

WHAT WE CLAIM IS:—

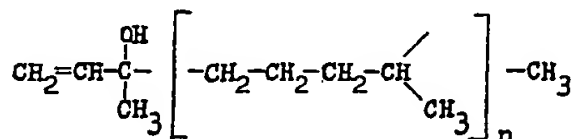
- 15 1) Aliphatic triols of the formula



, wherein  $n$  is 1,2 or 3.

- 2) 3,7,11,15 - Tetramethyl - 1,2,3 - trihydroxy-hexadecane.
- 20 3) 3,7,11 - Trimethyl - 1,2,3 - trihydroxy-dodecane.
- 4) 3,7 - Dimethyl - 1,2,3 - trihydroxy-octane.

- 25 5) A process for the manufacture of the triols claimed in claim 1 hereof, which process comprises reacting a compound having the formula:



, wherein  $n$  is 1,2 or 3, with an organic peracid in the presence of the carboxylic acid corresponding to said peracid and hydrolyzing the reaction product.

- 6) A process in accordance with claim 5, wherein the starting material is isophytol, tetrahydro-nerolidol or dihydro-linalool.

- 7) A process in accordance with claim 5 or claim 6, wherein the organic peracid is performic acid.

- 8) A process in accordance with claims 5,6 or 7, wherein the said peracid is formed *in situ* by the action of hydrogen peroxide on the corresponding carboxylic acid.

- 9) A process in accordance with any one of the preceding process claims, wherein the hydrolysis is carried out using concentrated ammonia.

- 10) A process for the manufacture of the aliphatic triols claimed in claim 1 hereof, substantially as described with reference to the examples.

- 11) Aliphatic triols as claimed in claim 1 hereof, when manufactured by the process claimed in any one of claims 5 to 10 inclusive.

- 12) A cosmetic preparation comprising one or more triols as claimed in claim 1 hereof and a compatible solid or liquid cosmetic excipient.

- 13) A preparation as claimed in claim 12, wherein said triol or triols is or are present in the preparation in a range of from 0.1 to 10 per cent by weight.

W. D. WHITAKER,  
Patent Agent,  
for F. Hoffmann-La Roche & Co.  
Aktiengesellschaft.